

CLAIMS

1. Non human transgenic animal, being transgenic for an antibody or fragments thereof and having a phenotype reminiscent of a human pathology.

2. A non-human transgenic animal according to claim 1 wherein the human pathology is included in the following group: neurodegenerative syndromes; muscular atrophy/dystrophy; immune disorders.

3. A non-human transgenic animal according to claim 2 wherein the human pathology is the Alzheimer disease (AD).

4. A non-human transgenic animal according to claim 3 exhibiting at least one of the anatomical, histological, molecular or phenotypic markers included in the following group: deposition in Central Nervous System (CNS) of plaques of amyloid precursor protein (APP) or of β -amyloid protein, hyperphosphorylation of the tau protein, neurofibrillar pathology, deficits in the cholinergic system.

5. A non-human transgenic animal according to claim 4 further exhibiting at least one of the anatomical, histological, molecular or phenotypic markers included in the following group: glial activation, neuronal loss, cortical and hippocampal atrophy, muscular myositis.

6. A non-human transgenic animal according to claim 5 exhibiting the following anatomical, histological, molecular or phenotypic markers: deposition in Central Nervous System (CNS) of plaques of amyloid precursor protein (APP) or of β -amyloid protein, hyperphosphorylation of the tau protein, neurofibrillar pathology, deficits in the cholinergic system, glial activation, neuronal loss, cortical and hippocampal atrophy, muscular myositis.

7. A non-human transgenic animal according to claim 6 exhibiting the anatomical, histological, molecular or phenotypic markers as defined in Table 1.

8. A non-human transgenic animal according to claim 7 wherein said markers are expressed in the adult age.

5 9. A non-human transgenic animal according to claim 7 wherein the occurrence of the tau hyperphosphorylation and/or the β -amyloid protein deposition in the back or lower limb skeletal muscles and/or the atrophy of said skeletal muscles are present concomitantly to the earliest occurrence of other neurological markers.

10 10. A non-human transgenic animal according to any of previous claims being transgenic for an anti-NGF (Nerve Growth Factor) antibody or fragment thereof.

11. A non-human transgenic animal according to claim 10 wherein the anti-NGF antibody blocks the binding of NGF to its receptors.

12. A non-human transgenic animal according to claim 10 wherein the anti-NGF antibody is expressed mainly in the adulthood.

15 13. A non-human transgenic animal according to claim 12 wherein the anti-NGF antibody levels in the serum of the adult animal are comprised between 50 ng/ml and 500 ng/ml.

14. A non-human transgenic animal according to claim 10 wherein the anti-NGF antibody is the monoclonal anti-NGF α D11 antibody.

20 15. A non-human transgenic animal according to claim 14 wherein the α D11 antibody is a α D11 chimeric antibody.

16. A non-human transgenic animal according to claim 15 wherein the chimeric antibody is a humanised chimeric antibody.

25 17. A non-human transgenic animal according to any of previous claims wherein the animal is a mammalian.

18. A non-human transgenic animal according to claim 17 belonging to the murine genus.

19. A non-human transgenic animal according to claim 18 belonging to the *Mus musculus* BS6JL strain.

20. A method for an early diagnosis of neurodegenerative diseases comprising the monitoring of the occurrence of the tau hyperphosphorylation and/or amyloid deposition in the back or lower limb skeletal muscle sample of a subject.

5 21. Cells derivable from the non-human transgenic animal according to any of claims 1-19 and secreting the transgene antibody.

22. Use of cells according to claim 21 for the selection of molecules pharmacologically effective in neurodegenerative and/or muscular pathologies and/or immune disorders.

10 23. Use of cells according to claim 21 for the grafting in the brain of a non human primate.

24. Method for the preparation of a non-human transgenic animal according to claim 1 comprising essentially the steps of:

15 a) preparing a first non-human transgenic parent animal for the light chain of an antibody and a second non-human transgenic parent animal for the heavy chain of the same antibody,

b) breeding the two transgenic parent animals;

c) selecting the progeny expressing both the light and the heavy chain.

20 25. Method for the preparation of a non-human transgenic animal according to claim 10 comprising essentially the steps of:

a) preparing a first non-human transgenic parent animal for the light chain of an anti-NGF antibody and a second non-human transgenic parent animal for the heavy chain of an anti-NGF antibody,

25 b) breeding the two transgenic parent animals;

c) selecting the progeny expressing both the light and the heavy chain.

26. Use of the non-human transgenic animal according to claim 2 for the study of neurodegenerative syndromes.

27. Use of the non-human transgenic animal according to claim 2 for the study of pathologies of muscular system.

28. Use of the non-human transgenic animal according to claim 3 for the study of Alzheimer's disease.

5 29. Use of the non-human transgenic animal according to claim 2 for the selection of compounds pharmacologically effective in the treatment of pathologies included in the following group: neurodegenerative syndromes; muscular atrophy/dystrophy, immune disorders.

10 30. Use of the non-human transgenic animal according to claim 3 for the selection of compounds pharmacologically effective in the treatment of the Alzheimer's disease.

31. Use of the non-human transgenic animal according to claim 10 for the study of pathologies related to an NGF deficit.

15 32. Use of the non-human transgenic animal according to claim 10 for the screening of compounds potentiating the activity of NGF.

33. Use of the non-human transgenic animal according to claim 10 for the screening of compounds stimulating the expression and/or the release of endogenous NGF.

20 34. Use of the non-human transgenic animal according to claim 10 for the screening of formulations of NGF or derivatives thereof able to cross the blood-brain barrier.

35. Use of NGF or of derivatives or fragments thereof for the preparation pharmaceutical compositions able to bind autoanti-NGF antibodies in the brain of AD affected subjects.

25 36. Use of NGF or of derivatives or fragments thereof for the preparation of pharmaceutical compositions for the treatment of muscular pathologies.

37. Pharmaceutical compositions including NGF (Nerve Growth Factor) for the therapy of the muscular pathologies.